REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Claim Amendments

Claim 13 has been amended to recite a method of promoting neuritogenesis of corneal nerves that are damaged, cut or defective by a corneal surgery or corneal disease. Support for this amendment may be found on page 8, lines 14-25 of Applicants' specification.

Patentability Arguments

The patentability of the present invention over the disclosures of the references relied upon by the Examiner in rejecting the claim will be apparent upon consideration of the following remarks.

Rejection Under 35 U.S.C. § 103(a)

Claim 13 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Hellberg et al. (WO 03/020281) in view of McKerracher et al. (WO 99/23113) and Hara et al. (Protein kinase inhibition by fasudil hydrochloride promotes neurological recover after spinal cord injury in rats). This rejection is respectfully traversed.

Hellberg et al. teach a method comprising administering neurotrophic factor stimulators to a human patient, wherein the neurotrophic factor stimulators increase the production or activity of neurotrophic factors (NGF, BDNF, NT-3, bFGF etc.) to promote neuron regeneration or neurite outgrowth, wherein the method is useful for the treatment of dry eye and corneal nerve damage. That is, Hellberg et al. indicate that the treatment is influenced by "neurotrophy". However, the teachings of Hellberg et al. are not related to the inhibition of Rho kinase inhibitor, as admitted by the Examiner. The Examiner takes the unsupported position that it would have been obvious to use another neurite promoter, such as fasudil, for corneal injury since Hellberg et al. teach the use of compounds that promote neuron regeneration. However, there is no common technical knowledge that the mode of action of neurotrophic factors is the same as (or similar to) that of Rho kinase inhibitor. Therefore, contrary to the Examiner's general assertion,

one of ordinary skill in the art would not have been motivated to substitute a neurotrophic factor with a Rho kinase inhibitor in the method disclosed in Hellberg et al., with any reasonable expectation of a similar effect, even if the neurotrophic factor was effective.

Hara et al. teach that fasudil hydrochloride promotes neurological recovery after traumatic spinal cord injuries (SCI), as the results of histopathological tests of spinal cord, spinal cord blood flow study and behavioral tests of functional deficit. However, ***Hara et al. fail to teach or suggest that fasudil hydrochloride and other Rho kinase inhibitors promote corneal neuritogenesis.***

The corneal nerve is a trigeminal nerve, and is different from the spinal cord nerve. The Examiner contends that neurotrophic factors are also known as agents which improve neurological recovery after spinal cord injury (SCI). However, Hara et al. merely teach in the "Introduction" section that methylprednisolone can promote neurological recovery after SCI, and that a similar effect is known in some neurotrophic factors. Methylprednisolone is not a Rho kinase inihibitor, but rather a steroid drug. There is no common technical knowledge that the modes of action of neurotrophic factors and methylprednisolone are the same as (or similar to) that of Rho kinase inhibitor. Therefore, ***one of ordinary skill in the art would not have been motivated to substitute a neurotrophic factor with a Rho kinase inhibitor in order to promote corneal neuritogenesis, with any reasonable expectation of a similar effect, even if the neurotrophic factor was effective for promoting neurological recovery after SCI***.

McKerracher et al. disclose that a Rho antagonist (e.g., C3 enzyme) has the effect of retinal neurite extension, retinal ganglion cell axon growth and optic nerve regeneration. However, there is no teaching or suggestion that the compounds described in claim 13 of the present application promote corneal neuritogenesis. The corneal nerve is a trigeminal nerve, and is distinct from the retinal nerve. Therefore, ***one of ordinary skill in the art would not have been motivated to substitute a Rho antagonist with any of the Rho kinase inhibitors recited in claim 13 in order to promote corneal neuritogenesis, with any reasonable expectation of success, even if the Rho antagonist was effective for promoting retinal neurite extension and the like***.

It is clear from the discussion above that the subject matter of Applicants' claims is not rendered obvious by the combination of references provided. Hellberg et al. disclose compounds

for neuron regeneration and neurite outgrowth, but these compounds are distinct from the compounds of Applicants' claims. Hara et al. disclose fasudil hydrochloride as promoting neurological recovery after a spinal cord injury, but the reference makes no mention of corneal neuritogenesis, and the corneal nerve is distinct from the spinal cord nerve. Lastly, McKerracher et al. disclose Rho antagonists as effecting retinal neurite extension, retinal ganglion cell axon growth and optic nerve regeneration, but fails to teach or suggest the compounds recited in Applicants' claims, and fails to teach promotion of corneal neuritogenesis.

For these reasons, the invention of claim 13 is clearly patentable over the cited combination of references. Withdrawal of the rejection is respectfully requested.

Conclusion

Therefore, in view of the foregoing amendments and remarks, it is submitted that the ground of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Amendment, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

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